Trop2 as a new driver of castration-resistant prostate cancer

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Background: Trop2 is a cell surface glycoprotein that is commonly altered in a broad range of epithelial cancers. Due to its overexpression in multiple epithelial cancers, Trop2 has emerged as a promising therapeutic target. An anti-Trop2 antibody conjugated with cytotoxic drug SN-38, Sacituzumab govitecan (IMMU-132), has been recently developed and has shown a promising therapeutic effect in triple negative breast and other cancers. Currently, IMMU-132 is being evaluated as a single agent in patients with advanced epithelial cancers including CRPC.

Methods: To assess the functional role of Trop2 in prostate cancer cell growth and androgen independence *in vitro*, we used colony formation, tumorsphere and proliferation assays. To evaluate the role of Trop2 in castration-resistant prostate cancer (CRPC) *in vivo*, we utilized prostate cancer xenograft models. Trop2 deletion was achieved via CRISPR/Cas9 and overexpression via lentiviral transduction.

Results: Our results demonstrate that Trop2 level is elevated in castration-resistant prostate cancer (CRPC) and metastatic prostate cancer. High level of Trop2 is associated with higher risk of recurrence of prostate cancer. Our study demonstrates that loss of Trop2 significantly delays growth, migration and invasion of prostate cancer cells. Loss of Trop2 gene suppresses tumor growth *in vivo* while overexpression of Trop2 enhances prostate cancer cell invasion and tumor growth. Moreover, overexpression of Trop2 induces androgen independent prostate cancer cell growth and drives castration-resistant prostate cancer *in vivo*.

Conclusions: Our results demonstrate that Trop2 plays a functional role in prostate cancer and drives CRPC. These findings provide a strong functional evidence that Trop2 may represent a new rational therapeutic target for metastatic CRPC.

Conflict of Interest: None

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